

## CLAIMS:

1. A composition comprising a reaction mixture comprising a complex of an NS1 protein of influenza virus, or a dsRNA binding fragment thereof, and a dsRNA that binds said protein.
- 5 2. The composition of claim 1, wherein said NS1 protein is an NS1 protein of Influenza A (NS1A).
3. The composition of claim 2, comprising a dsRNA binding domain of said NS1A protein.
4. The composition of claim 3, wherein said dsRNA binding  
10 fragment comprises amino acid residues 1-73 of NS1A.
5. The composition of claim 1, wherein said NS1 protein is an NS1 protein of Influenza B (NS1B).
6. The composition of claim 5, comprising a dsRNA binding domain of said NS1 B protein.
- 15 7. The composition of claim 6, wherein said dsRNA binding fragment comprises amino acid residues 1-93 of NS1B.
8. The composition of claim 1, wherein said dsRNA has a length of about 16 base pairs.
9. The composition of claim 1, wherein said dsRNA binding  
20 portion comprises amino acid residues 1-73 of NS1A, and wherein said dsRNA has a length of about 16 base pairs.
10. The composition of claim 1, wherein said dsRNA binding portion comprises amino acid residues 1-93 of NS1B, and wherein said dsRNA has a length of about 16 base pairs.
- 25 11. The composition of claim 1, further comprising a compound being tested for inhibitory activity against influenza virus.
12. The composition of claim 1, wherein the NS1 protein or the dsRNA is detectably labeled.
13. A method of identifying compounds having inhibitory  
30 activity against an influenza virus, comprising:
  - a) preparing a reaction system comprising an NS1 protein of an influenza virus or a dsRNA binding domain

thereof, a dsRNA that binds said protein or binding domain thereof, and a candidate compound; and

b) detecting extent of binding between the NS1 protein and the dsRNA, wherein reduced binding between the NS1 protein and the dsRNA in the presence of the compound relative to a control is indicative of inhibitory activity of the compound against the influenza virus.

14. The method of claim 13, wherein the NS1 protein or dsRNA binding domain thereof is immobilized on a solid support.

15. The method of claim 13, wherein the candidate compound is added to the reaction system prior to or simultaneously with the NS1 protein and the dsRNA.

16. The method of claim 13, wherein the candidate compound is added to the reaction system subsequent to addition of the NS1 protein and the dsRNA.

17. The method of claim 13, further comprising labeling the dsRNA, NS1 protein or dsRNA binding domain thereof with a detectable label, prior to said detecting.

18. The method of claim 17, wherein the detectable label comprises an antibody or fragment thereof that binds the NS1 protein or dsRNA binding domain thereof.

19. The method of claim 17, wherein the detectable label comprises an enzyme and the reaction system further comprises a substrate for the enzyme.

20. The method of claim 17, wherein the detectable label comprises a radioisotope.

21. The method of claim 17, wherein the detectable label comprises a fluorescent label.

22. The method of claim 13, wherein said detecting is conducted via fluorescent resonance energy transfer.

23. The method of claim 13, wherein said detecting is conducted via fluorescence polarization anisotropy measurements.

24. The method of claim 13, wherein the NS1 protein or dsRNA binding fragment thereof is present in the reaction system as a fusion protein with glutathione-S-transferase.

25. The method of claim 13, wherein said NS1 protein is a NS1  
5 A protein.

26. The method of claim 13, wherein said NS1 protein is a NS1  
B protein.

27. The method of claim 13, wherein the reaction system  
comprises a fragment of the NS1 protein comprising a dsRNA binding  
10 domain of said NS1 protein.

28. The method of claim 27, wherein the dsRNA binding domain  
comprises NS1A (1-73).

29. The method of claim 27, wherein the dsRNA binding domain  
comprises NS1B (1-93).

30. The method of claim 13, wherein the dsRNA has a length of  
15 about 16 base pairs.

31. The method of claim 13, wherein the method of  
identification comprises a high throughput screening assay.

32. A method of identifying compounds having inhibitory  
20 activity against an influenza virus, comprising:

a) preparing a reaction system comprising an NS1  
protein of an influenza virus or a dsRNA binding domain  
thereof, a dsRNA that binds said protein or binding domain  
thereof, and a candidate compound;

25 b) detecting extent of binding between the NS1 protein  
and the dsRNA, wherein reduced binding between the NS1 protein  
and the dsRNA in the presence of the compound relative to a  
control is indicative of inhibitory activity of the compound  
against the influenza virus; and

30 c) determining extent of a compound identified in b) as  
having inhibitory activity to inhibit growth of influenza  
virus in vitro.

33. The method of claim 32, wherein the method of identifying compounds having inhibitory activity is selected from the group consisting of (a) NMR chemical shift perturbation, (b) gel filtration chromatography, or (c) sedimentation equilibrium measurements using an analytical ultracentrifuge.

34. The method of claim 32, further comprising d) determining extent of a compound identified in c) as inhibiting growth of influenza virus *in vitro*, to inhibit replication of influenza virus in a non-human animal.

35. A method of preparing a composition for inhibiting replication of influenza virus *in vitro* or *in vivo*, comprising:

a) preparing a reaction system comprising an NS1 protein of an influenza virus or a dsRNA binding domain thereof, a dsRNA that binds said protein or binding domain thereof, and a candidate compound;

b) detecting extent of binding between the NS1 protein and the dsRNA, wherein reduced binding between the NS1 protein and the dsRNA in the presence of the compound relative to a control is indicative of inhibitory activity of the compound against the influenza virus;

c) determining extent of a compound identified in b) as having inhibitory activity to inhibit growth of influenza virus *in vitro*;

d) determining extent of a compound identified in c) as inhibiting growth of influenza virus *in vitro*, to inhibit replication of influenza virus in a non-human animal; and

e) preparing the composition by formulating a compound identified in d) as inhibiting replication of influenza virus in a non-human animal, in an inhibitory effective amount, with a carrier.

36. The method of claim 35, further comprising f) determining the inhibitory effective amount of the compound on the basis of results obtained from c) and d).

37. The method of claim 35, wherein the carrier is suitable for administration to an animal via inhalation or insufflation.

38. A method of identifying a compound for use as an inhibitor of influenza virus comprising:

(a) obtaining coordinates for a three-dimensional structure of the influenza virus NS1 protein;

(b) selecting a potential compound by performing rational drug design with said coordinates for a three-dimensional structure obtained in step (a), wherein said selecting is performed in conjunction with computer modeling of an NS1-dsRNA complex;

(c) contacting the potential compound with a influenza virus; and

(d) measuring the activity of the influenza virus; wherein a potential compound is identified as a compound that inhibits influenza virus when there is a decrease in the activity of the influenza virus in the presence of the compound relative to in its absence.

39. The method of claim 38, wherein the NS1 protein is a NS1A protein or a dsRNA binding domain thereof.

40. The method of claim 39, wherein dsRNA binding domain is NS1A (1-73).

41. The method of claim 38, wherein the NS1 protein is a NS1B protein or a dsRNA binding domain thereof.

42. The method of claim 41, wherein dsRNA binding domain is NS1B (1-93).